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For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: **ENHANCEMENT OF BACTERICIDAL ACTIVITY OF NEISSERIA ANTIGENS WITH OLIGONUCLEOTIDES
CONTAINING CG MOTIFS**

(57) Abstract: Immunogenic compositions (e.g. vaccines) comprising: (a) an immunostimulating amount of a Neisseria antigen (preferably N. meningitidis serogroup B); and (b) an immunostimulating amount of an adjuvant composition comprising an oligonucleotide comprising at least one CG motif. Component (b) may further comprise a second adjuvant. Component (a) may be selected from a variety of antigens. Adjuvant compositions comprising an oligonucleotide having at least one CG motif, and complete Freund's adjuvant (CFA) are also provided.

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INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference P023888W0	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/IB 00/00176	International filing date (day/month/year) 09/02/2000	(Earliest) Priority Date (day/month/year) 26/02/1999
Applicant CHIRON S.P.A. et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.
☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing:
- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☒ furnished subsequently to this Authority in written form.
- ☒ furnished subsequently to this Authority in computer readable form.
- ☒ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☒ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☒ **Unity of invention is lacking** (see Box II).

4. With regard to the title,

- ☒ the text is approved as submitted by the applicant.
- ☐ the text has been established by this Authority to read as follows:

5. With regard to the abstract,

- ☐ the text is approved as submitted by the applicant.
- ☒ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No.

- ☐ as suggested by the applicant.
- ☐ because the applicant failed to suggest a figure.
- ☐ because this figure better characterizes the invention.
- ☐ None of the figures.

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national application No.

PCT/IB 00/00176

Box III TEXT OF THE ABSTRACT (Continuation of item 5 of the first sheet)

Immunogenic compositions (e.g. vaccines) comprising: (a) an immunostimulating amount of a Neisseria antigen (preferably N. meningitidis serogroup B); and (b) an immunostimulating amount of an adjuvant composition comprising an oligonucleotide comprising at least one CG motif. Component (b) may further comprise a second adjuvant. Component (a) may be selected from a variety of antigens. Adjuvant compositions comprising an oligonucleotide having at least one CG motif, and complete Freund's adjuvant (CFA) are also provided.

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A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K39/095 A61K39/39 A61P31/04 //C12N15/31,C07K14/22

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

STRAND, MEDLINE, BIOSIS, EPO-Internal, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
<input checked="" type="checkbox"/>	<p>WO 98 18810 A (UNIV IOWA RES FOUND ;KLINE JOEL N (US); KRIEG ARTHUR M (US)) 7 May 1998 (1998-05-07)</p> <p>page 11, line 12 page 10, line 16-23 page 17, line 8,9 page 27, line 23 claims 23,26</p>	<p>1-4, 18-21, 23, 32-37, 40-42</p>
<input checked="" type="checkbox"/>	<p>WO 98 49288 A (HYBRIDON INC) 5 November 1998 (1998-11-05)</p> <p>page 4, paragraph 2 page 12, paragraph 2</p>	<p>1-4, 18-21, 23, 32-37, 40-42</p>
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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

4 October 2000

Date of mailing of the international search report

17/10/2000

Name and mailing address of the ISA

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
✓ X	WO 98 55495 A (DYNAVAX TECHNOLOGIES CORP ;DINA DINO (US); ROMAN MARK (US); SCHWAR) 10 December 1998 (1998-12-10) page 15, line 5-25 examples 1,2 claim 23	27-31, 40,41
A	--- SUN SIQUAN ET AL: "DNA as an adjuvant: Capacity of insect DNA and synthetic oligodeoxynucleotides to augment T cell responses to specific antigen." JOURNAL OF EXPERIMENTAL MEDICINE, vol. 187, no. 7, ✓ 6 April 1998 (1998-04-06), pages 1145-1150, XP002148907 ISSN: 0022-1007 abstract page 1146, left-hand column, line 1-5 -right-hand column, line 5-10	6-17,24, 27
A	--- MILLAN CYNTHIA L BRAZOLOT ET AL: "CpG DNA can induce strong Th1 humoral and cell-mediated immune responses against hepatitis B surface antigen in young mice." PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES, vol. 95, no. 26, ✓ 22 December 1998 (1998-12-22), pages 15553-15558, XP002148908 Dec. 22, 1998 ISSN: 0027-8424 abstract figure 2	6-17,24, 27
✓ P,X	--- WO 99 58683 A (RUELLE JEAN LOUIS ;SMITHKLINE BEECHAM BIOLOG (BE)) 18 November 1999 (1999-11-18) cited in the application page 31, line 14 -page 36, line 24	1-4,6, 18,20, 22-24, 26, 32-37, 40-42
✓ A,P	--- WO 99 57280 A (PIZZA MARIAGRATIA ;MORA MARIROSA (IT); RAPPUOLI RINO (IT); GALEOTT) 11 November 1999 (1999-11-11) cited in the application page 135 example 15 -----	5,25,38

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-26 32-39 (all completely) 40-42 (all partially)

An immunogenic composition comprising a Neisseria antigen and an adjuvant composition comprising an oligonucleotide comprising at least one CG motif and, optionally, a second adjuvant.

2. Claims: 27-31 (all completely) 40-42 (all partially)

An adjuvant composition comprising at least one CG motif and complete Freund's adjuvant and any antigen other than Neisseria

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International application No.
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Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 32-39 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☒ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/IB 00/00176

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9818810 A	07-05-1998	AU 5242498 A CN 1235609 A EP 0948510 A	22-05-1998 17-11-1999 13-10-1999
WO 9849288 A	05-11-1998	AU 7171298 A EP 0991755 A	24-11-1998 12-04-2000
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WO 9958683 A	18-11-1999	AU 4142099 A	29-11-1999
WO 9957280 A	11-11-1999	AU 3967799 A	23-11-1999